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A Review of Hexachlorocyclopentadiene Adducts Intended for Use as Flame Retardants

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Cat. No. En 40-3/83-12
ISBN 0-662-12191-8

A REVIEW OF HEXACHLOROCYCLOPENTADIENE ADDUCTS INTENDED FOR USE AS FLAME RETARDANTS

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EPS 3-EC-82-4

Disponible en français

s'adresser au:

Coordonnateur des publications
Direction générale du contrôle des incidences environnementales
Service de la protection de l'environnement
Environnement Canada
Ottawa (Ontario)
K1A 1C8

et demander:

"Les composés d'addition de l'hexachlorocyclopentadiene, produits ignifuges"

ABSTRACT

This review, completed in 1980, examines information on the amounts of hexachlorocyclopentadiene adducts imported, used, exported or disposed of, and on the amounts used in various commercial activities. Information on the levels in various ecosystems and on the sources and modes of entry into the various sectors of the Canadian environment is also examined. On the basis of these examinations, information gaps are identified, taking into consideration other relevant observations.

RÉSUMÉ

Cette étude, complétée en 1980, examine les donées relatives aux quantités d'hexachlorocyclopentadiène (HCCPD) importées, exportées ou éliminées et celles qui sont utilisées, notamment dans diverses activités industrielles. Leur concentration dans divers écosystèmes, leur origine et leur mode de pénétration dans différents secteurs de l'environnement canadien font aussi l'objet de cet examen. Les lacunes dans les données existantes sont relevées, compte tenu des observations pertinentes qui ont été faites à ce sujet.

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SUMMARY OF RECOMMENDATIONS

1. More information should be collected using the provision of the Environmental Contaminants Act concerning the quantities of Dechloranes in Canadian commerce.
2. A detailed protocol for Dechloranes should be formulated to describe the following areas of investigations that should be undertaken:
   - 2.1 toxicological testing;
   - 2.2 physicochemical properties required for the assessment of chemodynamic characteristics;
   - 2.3 accumulation of the material in aquatic organisms and the possibility of subsequent human exposure; and
   - 2.4 methodology for investigation of leaching from plastics.
3. The quantities of Dechloranes discharged in effluents and emissions from industrial plants should be investigated. Methods for the safe disposal of these kinds of compounds should be examined.
4. An epidemiological investigation of workers that are occupationally exposed to Dechloranes should be undertaken.

1 INTRODUCTION

Hexachlorocyclopentadiene (HCCPD) is a versatile chemical intermediate whose products have had a widespread impact on technology and the environment. HCCPD reacts with a large number of other unsaturated organic compounds to yield additional products. The adducts so formed include compounds that have been used as pesticides or as flame retardant additives to synthetic polymers; others have been proposed as additives in extreme pressure lubricants or as reactive intermediates (monomers) for preparation of flame retardant polymeric resins.

This review is concerned with hexachlorocyclopentadiene adducts, other than mirex, that have been used or proposed as flame retardant additives for synthetic polymers. Mirex is not included in this review, since following its identification as a contaminant in fish from Lake Ontario (Kaiser, 1974) it has been assessed and regulated under the Environmental Contaminants Act. A summary of the findings of the "Task Force on Mirex" are provided as background information (see Section 1.1). The purpose of this document is to review the information available on certain other flame retardant HCCPD adducts, to enable the DOE/NH&W Toxic Chemicals Committee to decide whether controls are desirable, or whether further information is needed.

1.1 The Task Force on Mirex

In 1976 a Task Force set up by the DOE/NH&W Environmental Contaminants Committee, enquired into the substance mirex. All uses of mirex in Canada were subsequently prohibited under the Environmental Contaminants Act (Canada Gazette Part II, Vol. 112, No. 23, p. 43). The Task Force report, "Mirex in Canada" published in 1977, expressed concern about the environmental acceptability of other lipid soluble adducts of HCCPD and particularly the series described below. Their concern was based on the analogies between the chemical structures or properties of the flame retardants (mirex and kepone) and those of the cyclodiene insecticides (e.g. aldrin). Hexachlorocyclopentadiene and its adducts were thus placed on the List of Priority Chemicals (Canada Gazette Part I, May 20, 1978, p. 3011) that should be investigated under the Environmental Contaminants Act.

The Task Force on Mirex reviewed the evidence concerning levels of contamination by mirex in various Canadian ecosystems. Though mirex had been detected in most organisms where it had been sought, the levels in most locations were extremely low. A

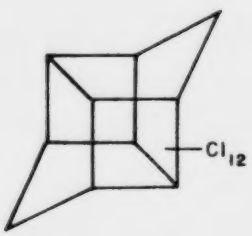
serious problem of environmental contamination with mirex was found in Lake Ontario. Lake Ontario fish were the presumed source of contamination of the Great Lakes herring gulls Larus argentatus and their eggs. Mirex (7.2 ppm) was the third highest organochlorine residue in Lake Ontario herring gull eggs after polychlorinated biphenyls; (PCBs; 204 ppm) and dichloro diphenyldichloroethylene (DDE; 34 ppm). The sediment data showed that mirex entered the lake from the Niagara River and extended eastward as a plume along the south shore. A second source was indicated with its origins in Oswego, New York. It was estimated that only 700 kg of mirex and 350 kg of photomirex, a presumed degradation product of mirex, were in the Lake Ontario sediments. The Task Force reported two major Canadian users of mirex - Inmont Presstite Ltd. of Georgetown, Ontario (reputedly 117 285 kg), and Kayson Plastics Div., Polysar Ltd., Cambridge, Ontario (13 752 kg). Though these users were not known to have contributed to the contamination of Lake Ontario, the DOE/NH&W Environmental Contaminants Committee decided that further use of mirex would constitute a significant danger. The decision was based on the consideration of the persistence, accumulation and biological effects of this substance.

1.2 Identity of HCCPD Flame Retardants

Three chemical companies are known to have produced flame retardant polymer additives based on HCCPD. Hooker Chemical Corporation has manufactured and sold a series of such compounds under the trade mark "Dechlorane". Cities Service Company produced "Citex BC-26" and Chemetron produced a series of compounds under the name "Fire Shield". Though the proportions of various structural isomers and impurities in the commercial products are not necessarily known, the following descriptions and diagrammatic structures of the compounds are provided.

1.2.1 Dechloranes. Mirex was marketed as a flame retardant additive under the names Dechlorane 510 and 4070. It is formed by the dimerization of HCCPD and its structure is shown below. Analysis by gas chromatography-mass spectroscopy (GC-MS) has shown that impurities are not present in analysed samples of this compound (Moniteq Ltd., 1977; Zitko, unpublished ms.).

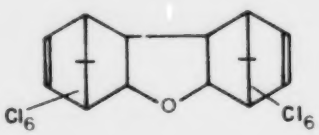
Dechlorane (mirex)



Dechlorane Plus has largely superseded mirex as a flame retardant in polymer systems because of its lower vapour pressure, lower specific gravity and lower solubility. It is the product from the reaction of HCCPD with cyclooctadiene (Mirex Task Force Report, 1977). Dechlorane Plus is available in two forms: as Dechlorane Plus 515 with a particle size between 5 and 15 microns, and as Dechlorane Plus 25 with a mean particle size between 2 and 5 microns. A gas chromatogram of Dechlorane Plus 25 contained two major peaks in an area ratio of 1:4. Both peaks had identical mass spectra and could be the endo-, exo- isomers. In addition, this product contains a minor impurity with a considerably shorter retention time on GC, and the only prominent ions in the mass spectrum were chlorocyclopentadiene ions (Zitko, unpublished ms.). Information is not available on Dechlorane Plus 515, but it is believed to be similar.

Dechlorane Plus

Dechlorane 602 is formed from the reaction of two molecules of HCCPD with a molecule of furan (Mirex Task Force Report, 1977). Samples of this compound did not contain peaks of impurities when analysed by GC-MS. It is said to be especially effective in elastomers to achieve fire retardance with minimum sacrifice of mechanical properties.



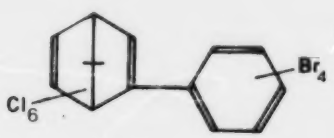
Dechlorane 602

Dechlorane 603 is an experimental fire retardant that is especially effective in applications requiring polymer processing temperatures approaching 316°C. It is formed from the addition reaction of two moles of HCCPD with one mole of bicycloheptadiene

(Mirex Task Force Report, 1977). The gas chromatogram of Dechlorane 603 contained only the peak of the major component (Zitko, unpublished ms).

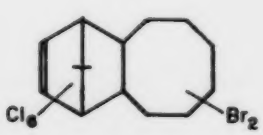
Dechlorane 603

Dechlorane 604 is especially effective in applications with styrene based polymers and copolymers, including polystyrene, ABS, and high impact polystyrene. It is formed from the addition reaction of 2,3,4,5-tetrabromostyrene with HCCPD (Mirex Task Force Report, 1977). The gas chromatogram of Dechlorane 604 contained peaks of three minor impurities with retention times (relative to that of the main component) of 0.67, 0.79, and 0.90, respectively. The first impurity (0.67) may be a tribomo analogue of Dechlorane 604. The identity of the other impurities could not be determined (Zitko, unpublished ms).



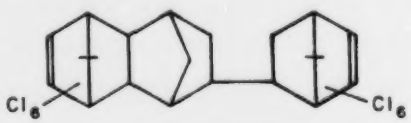
Dechlorane 604

1.2.2 Citex BC-26. Cities Service Company made Citex BC-26, which is formed by the bromination of the addition product of HCCPD and cyclooctadiene (D. Friedman, EPA, pers. comm.).



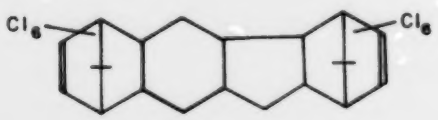
Citex BC-26

1.2.3 Fire Shields. Three Fire Shields designated C-1, C-2 and C-3 were produced by Chemetron. Addition of HCCPD to a vinyl norbornene yielded Fire Shield C-1 (P. Lombardo, FDA, pers. comm.).



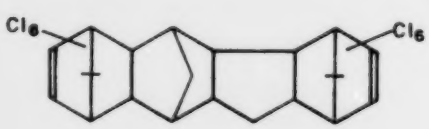
Fire Shield C-1

C-2 was formed from the addition reaction of HCCPD with the appropriately fused bicyclononadiene (P. Lombardo, FDA, pers. comm.).



Fire Shield C-2

C-3 was formed from the addition of HCCPD to dicyclopentadiene (P. Lombardo, FDA, pers. comm.).



Fire Shield C-3

1.3 Additional Information Sources

The production of this report has been aided not only by the existence of extensive information in the "Task Force on Mirex" report, but also by a major study on use of Dechloranes in Canada (Pascoe, unpublished ms.). On September 24, 1977, a notice

was published pursuant to subsection 4(1) of the Environmental Contaminants Act, which requires any person engaged in any commercial, manufacturing or processing activity involving Dechloranes to notify the Minister of the Environment. The Ontario Region of the Environmental Protection Service was designated the contact point for these notifications.

In Japan, testing was undertaken to investigate the bioaccumulation and persistence of Dechlorane Plus. Further work on bioaccumulation was undertaken in Canada by Dr. V. Zitko of the Department of Fisheries and Oceans, St. Andrews, New Brunswick.

The third edition of the Kirk-Othmer Encyclopedia of Chemical Technology lists only Dechlorane Plus, Het acid and Het anhydride flame retardant chemicals made (Hooker Chemicals and Plastics Corporation) from HCCPD. It does not appear that any new compounds have become important commercially.

2 HCCPD IN COMMERCE

2.1 Amounts Imported, Used and Exported

2.1.1 Dechloranes. On September 24, 1977, a notice was published in the Canada Gazette requiring any person engaged in any commercial, manufacturing or processing activity involving Dechlorane Plus, Dechlorane 602, Dechlorane 603 and Dechlorane 604 to notify the Minister of the Environment. The Ontario regional office of the Environmental Protection Service (EPS) was responsible for compiling a report concerning Dechlorane use in Canada. The EPS regional office contacted the Hooker Chemical corporation, Niagara Falls, NY, and received a list of Canadian clients and of the quantities of Dechlorane that had been sold in Canada. These figures suggest that in the period 1966-1977 the quantity of Dechlorane Plus imported into Canada was about 200 tonnes, and that only minor quantities (<2 tonnes) of Dechlorane 602 or 604 had been imported.

2.1.2 Citex BC-26 and Fire Shields. There are no data concerning Canadian importation or use of Citex BC-26 or Chemetron Fire Shields C-1, C-2 or C-3.

Dechloranes are not manufactured in Canada and there are, therefore, no bulk exports. Dechloranes have been incorporated into products manufactured in Canada; possibly a fraction of these was exported to the United States as finished products or as replacement parts. No detailed figures on the quantity exported in products are available.

2.2 Amounts of Waste HCCPD Adducts

Details of the operations at the Inmont Presstite Ltd. and the Kayson Plastics Division, Polysar Ltd. plants have been described in the Task Force on Mirex report (p. 27). Responses to the Canada Gazette notice revealed that a considerable number of other firms have small quantities of Dechloranes as inventory or awaiting disposal, or they have returned unused quantities to Hooker Chemical Corporation at Niagara Falls, NY.

2.3 Amounts Used in Various Commercial Products and Activities

The formulations of the Kayson Plastics Division, Polysar Ltd., polypropylene and of the Inmont Presstite Ltd. expandable sealer were reviewed on p. 28 of the "Task Force on Mirex" report.

A contract was let to Moniteq Ltd. by the Contaminants Control Branch, Environmental Protection Service, to develop analytical methodology and analyse com

mercial products for Dechloranes. Moniteq Ltd. contacted Hooker Chemical Corporation, Niagara Falls, New York, to obtain a list of Canadian users of Dechloranes. Samples of products were then solicited from nine companies in Ontario and Quebec. Six companies donated samples and the Dechlorane content of their products was determined. A flame retardant polypropylene contained between 16.7% and 20% Dechlorane Plus or Dechlorane (mirex). A flame retardant rubber contained 6.7% Dechlorane Plus. Four samples of experimental flexible wire sheathing contained between 13.6% and 16.7% Dechlorane Plus or 13.4% Dechlorane 602. A sample of wire sheathing contained between 9.7% and 13.5% Dechlorane Plus. Four samples of automobile sealant contained between 3.0% and 5.8% Dechlorane Plus. No Dechloranes were found in any of the four samples of flame retardant yarn.

2.4 Summary

Dechlorane Plus is the major product of this class of compounds that has been imported for use as a fire retardant. The detailed survey of Dechlorane use in Canada has revealed that several companies have small quantities in inventory and that some material has been returned to the manufacturer, the Hooker Chemical Corporation at Niagara Falls, NY. An analytical survey of products has shown that the Dechlorane content of polymers can be analysed using gas chromatography and mass spectrometry. At the time of the survey of Dechlorane use, supply difficulties distorted the market picture; companies known to have used Dechloranes have been requested to provide further information about usage in the last several years.

3 HCCPD IN THE ENVIRONMENT

3.1 Sources, Levels, and Modes of Entry

A detailed description of the investigations into the presence of Dechloranes in Ontario was included in the 1977 report of the "Task Force on Mirex" (p. 66). No further information has become available concerning the presence of Dechloranes in the Canadian environment thus the appropriate section from the Task Force report is excerpted, in part, below:

> "During investigations of the Inmont Presstite plant, at Georgetown in November, 1976, MOE staff collected water and sediment samples from several locations in the Credit River through Georgetown; in Silver Creek, a tributary of the Credit River flowing through Georgetown; and, in a storm-water ditch flowing adjacent to the Inmont Presstite plant. Sediment and seepage samples from several locations in the two solid waste disposal sites, and samples of raw and treated sewage from the Georgetown STP were also collected."
>
> "Results of analyses carried out by MOE show that .... Dechlorane Plus was detected in water samples in the Credit River at levels up to 0.1 ppb, and in seepage from the landfills it was found at levels up to 0.6 ppb. Only one location was found where there was a residue of Dechlorane Plus in sediment and that was in the ditch adjacent to the Inmont Presstite Ltd. factory. Additional sampling is to be undertaken to determine the extent of detectable levels in this area."
>
> "During investigation of the Polysar Ltd. plant at Cambridge in late October and through November, 1976, MOE staff collected water and sediment samples from the Speed River, as well as seepage and sediment samples from the vicinity of the abandoned Russ Street landfill site (closed in 1971). Soil and water samples were collected near the Kayson Plastics plant site. Raw and treated water from the Brantford Water Works (downstream from Cambridge) was also collected and analysed for Dechlorane Plus."
>
> "Results, to date, of analyses carried out by MOE and the Ontario Ministry of Agriculture and Food show that .... Dechlorane Plus was detectable in seepage from the former landfill at Russ Street at levels up to 0.089 ppb. River

sediment from 1500 yards below the former landfill contained 36 ppb. Tests on the water supply at Brantford, both raw water and final treated water, showed no detectable residues of Dechlorane Plus."

"Despite the small quantities of Dechloranes 602 and 604 brought to the Polysar Ltd. plant both these substances were found in samples at the Russ Street landfill site. Two sediment samples in the eastern drainage ditch contained 4 and 8 ppb, respectively, of Dechlorane 602 and sediment from the river contained 12 ppb. Similarly, sediment samples from the east and west drains contained 8 ppb and 10 ppb, respectively, and seepage from the east ditch contained 0.028 ppb Dechlorane 604."

"The concentration found in the Credit River at Georgetown indicated that about 1.5 kilograms of Dechlorane Plus is entering this system per year, and that further investigation of the sources is needed."

About a gram per year of Dechlorane Plus is coming out of the Russ Street (Cambridge) landfill site, in addition to Dechlorane 602 and 604.

"Though these quantities are small they do warrant further work to document their significance to biota particularly because the levels in the sediments indicate that the concentration of Dechlorane Plus is comparable to levels of mirex in contaminated Lake Ontario sediments."

3.2 Other Observations

In Section 5.3.9 of the "Task Force on Mirex" report, the following rationale was given as to why HCCPD and its lipid soluble addition-products are unacceptable from an environmental standpoint and why consideration should be given to the feasibility of designating them a class of compounds, for the purposes of assessment, under the Environmental Contaminants Act.

"For many years it has been recognized that there are relationships between the biological properties of chemical compounds, their chemical structures and their physicochemical properties; these relationships are still not well understood. The Hansch approach (Gould, 1972) is a method of relating these properties within an homologous series. The toxicological, pharmacological, pharmacodynamic and environmental behaviour of other structurally related substances has been successfully predicted from a knowledge of their

physicochemical properties. For instance, the bioconcentration potential of organochlorine chemicals in fish was found to be closely correlated with the partition coefficients of the chemicals between n-octanol and water (Neely et al., 1974)."

"As has been noted in previous parts of this report, mirex is a dimer of hexachlorocyclopentadiene. Several other commercially important organochlorine alicyclic substances are synthesized from hexachlorocyclopentadiene by reactions involving olefins or dienes. Among these are the cyclodiene insecticides; aldrin, isodrin, chlordane, heptachlor, endrin, telodrin and dieldrin, and the fire retardants; Dechlorane (mirex), Dechlorane Plus, Dechlorane 602, Dechlorane 603 and Dechlorane 604."

"The structures of all these molecules are related in that they contain a five-carbon ring carrying six chlorine atoms. Kepone and mirex differ from the remainder in that they are cage-like structures and kepone contains a ketone group that easily forms ketals."

"The four characteristics of chemical compounds that stimulated the drafting and enactment of the Environmental Contaminants Act are persistence in the environment, capability for being dispersed in the environment at the molecular level, bioaccumulation and biological activity."

"The addition products of hexachlorocyclopentadiene listed above or their metabolites either have been shown or would be expected to exhibit these four characteristics. For instance, aldrin, dieldrin, endrin, chlordane, heptachlor, kepone and mirex are bioconcentrated in fish, birds and mammals. These substances are also carcinogenic in mammalian test systems and are persistent in the environment. In a microcosm study (Lu et al., 1975), hexachlorocyclopentadiene itself has been shown to accumulate in organisms and to be environmentaliy stable. It is also biologically active and could be dispersed in the environment."

"The structures of Dechlorane Plus, Dechlorane 602, Dechlorane 603 .... suggest that their behaviour in the environment will be similar to that of the other organochlorine substances."

The "Task Force on Mirex" concluded, in part, that:

1. "Very small amounts of both mirex and Dechlorane Plus are entering the Speed River at Cambridge. A low concentration of Dechlorane Plus was detected in the Credit River. The significance of these trace amounts has not been established."
2. "There are very few data by which to assess mirex (Dechlorane) substitutes. Structure-activity considerations indicate that many of these compounds prepared from hexachlorocyclopentadiene will have environmental properties similar to the cyclodiene insecticides."
3. "There is a need to assess the environmental significance of the other Dechloranes and the desirability of controls on their importation, use and disposal."

Since the "Task Force on Mirex" report was published in 1977, further research has been undertaken on the Dechloranes and this can be considered together with previously existing information under the following headings: toxicity, bioaccumulation, persistence and capability for dispersion in the environment.

3.2.1 Toxicity. The Hooker Chemical Corporation has undertaken toxicity studies on Dechlorane Plus, Dechlorane 602, Dechlorane 603 and Dechlorane 604. The company undertook acute oral, dermal, inhalation and ocular toxicity studies on all the compounds. In addition, for Dechlorane Plus it undertook a 90-day subacute feeding study in rats, a 28-day dermal study on albino rabbits, a 28-day inhalation study on rats, a skin sensitization study on guinea pigs and a 96-hour LC_{50} on young bluegill sunfish Lepomis macrochirus (see Appendix).

The results of the studies show that all these compounds are relatively non-toxic in these test systems. The studies do not, however, include tests that would be essential for a full assessment of these compounds. For example, there are no data concerning their mutagenic, teratogenic or carcinogenic potential, nor are there data on biochemical parameters such as hepatic microsomal enzyme induction. Some of these compounds have been used or produced for more than 10 years, but no data are available concerning the epidemiology for exposed workers. In addition, data are needed concerning the pharmacokinetics of these compounds.

3.2.2 Bioaccumulation. Three separate investigations have been undertaken on the bioaccumulation of Dechlorane Plus in fish. One was performed for Hooker Chemical Corporation in which bluegill sunfish were exposed in both static and flow-through test

systems. The second was undertaken by the Japanese Ministry of International Trade and Industry. The third investigation was undertaken by Dr. Vlado Zitko (Department of Fisheries and Oceans, St. Andrews, N.B.). It included studies of direct uptake from water and uptake from food in juvenile Atlantic salmon (Salmo salar) of Dechlorane Plus, 602, 603 and 604.

In the Hooker Chemical Corporation study, bluegill sunfish were exposed in a static system to an initial concentration of 1 ppm; however, levels were erratic over the test period. Dechlorane plus was accumulated rapidly from the test solution on the first seven days and remained relatively constant thereafter. It was concluded that some bioaccumulation takes place but the erratic water concentrations precluded calculation of a bioconcentration factor.

The second bioaccumulation study was conducted in a flow-through system in which a calculated amount of Dechlorane Plus was added at 90 second intervals. The nominal exposure concentration of Dechlorane Plus was 0.1 ppm in the test water (see Table 1). It was necessary to use a 1% v/v solution of acetone to maintain the test material at the 0.1 ppm level.

TABLE 1 30-DAY DYNAMIC BIOACCUMULATION STUDY IN BLUEGILL SUNFISH WITH DECHLORANE PLUS

Test Day	Dechlorane Plus Water (ppm)	Concentration Fish (ppm)	Magnification Factor
0	0.102	0.111	1.09
6	0.095	0.181	1.91
12	0.074	0.130	1.76
18	0.083	2.15*	25.9*
24	0.085	0.320*	3.76
30	0.069	0.385	5.58

* Attributed to experimental error due to contamination

The report from the Japanese Ministry claimed that Dechlorane Plus accumulated quickly during the test and then increased at a much lower rate and that the water concentration showed a small decrease over the test period. It concluded that Dechlorane Plus did bioaccumulate in fish during water exposure over a 30-day period. The

magnification factors reported are much lower than factors that are found for related organochlorine compounds such as mirex.

The Japanese methodology for the bioaccumulation test is set out in Article 7-2 of the "Law concerning the examination and regulation of manufacture, etc. of chemical substances." Carp are exposed in a flow-through system for up to eight weeks. Two or three test fish are analysed every one or two weeks during this period. The Japanese do not publish the actual bioaccumulation factors found but classify test compounds as 1) non-accumulative or low accumulative; 2) accumulated on a medium level; or 3) accumulated on a high level. Using this system Dechlorane Plus was classed as "non-accumulative or low accumulative."

In the Canadian studies by Dr. Zitko, the uptake and excretion of mirex, Dechlorane Plus 25, Dechloranes 602, 603, and 604, administered in water and, separately, in food to juvenile Atlantic salmon, was studied. The author concluded that:

> "Mirex and Dechlorane 602 are accumulated from water and from food. In both cases, the accumulation factors of mirex are similar to those of some tetrahalobiphenyls (Zitko, 1977) and a similar accumulation factor was found in a feeding experiment with coho salmon (Leatherland et al., 1979). Widespread use of mirex is likely to lead to a widespread contamination of aquatic biota. Such contamination has been observed as a result of the application of mirex as a pesticide (Water et al., 1977). Contamination of biota by Dechlorane 602 would not be as extensive because of the lower accumulation factors of this compound from water."
>
> "Dechloranes 603, 604, and Plus 25 were accumulated from food but not from water. The accumulation factors of Dechloranes 603 and 604 are similar to those observed with some dihalobiphenyls (Zitko, 1977) and the accumulation factor of Dechlorane Plus 25 is even lower. The lack of accumulation from water may limit the environmental contamination by these compounds, but the slow excretion rates may make any contamination very long-lasting. The Dechlorane 604 preparation used in this work contains an impurity that accumulates from food to a larger extent than Dechlorane 604."
>
> "The relatively low accumulation factors of the Dechloranes are probably caused by their high molecular weights and very low solubilities in water. It is likely that the reported "concentrations in water" of these compounds are

concentrations of molecular aggregates rather than concentrations of true solutions."

"On the basis of the available information, the risks associated with the use of Dechlorane Plus 25 as a flame retardant in plastics appear relatively low."

3.2.3 **Persistence.** Two studies have been undertaken to investigate the biodegradability of Dechlorane Plus. One was summarized in the Hooker Chemical Corporation technical trade memorandum and the second was undertaken by the Japanese Ministry of International Trade and Industry.

In the Hooker Chemical Corporation study, the material was dissolved in water-benzene mixtures and the benzene was then stripped from the solution leaving a preparation with a concentration of 4 mg/L. This was then placed in BOD bottles and mixed with settled domestic sewage seed, incubated, and the concentration of dissolved oxygen determined. The results showed no significant oxygen utilization; it was concluded that Dechlorane Plus was non-biodegradable in water.

The Japanese methodology for testing the biodegradability of chemical substances has been detailed in article 7-1 of the "Law concerning the examination and regulation of manufacture, etc., of chemical substances." The method uses a closed system apparatus for measuring oxygen consumption to which a culture of activated sludge is added. Using this methodology Dechlorane Plus was found to be non-biodegradable.

3.2.4 Capability for Dispersion in the Environment. The US EPA (1977 and 1978) developed a mathematical model to predict the likely fate and distribution of organic compounds in the aquatic environment. The model depends on data concerning the solubility, water/n-octanol partition coefficient, vapour pressure, photochemistry, sorption, hydrolysis rates, etc. The information available on Dechloranes is not sufficient to enable such a predictive analysis to be performed. Their low solubilities and low vapour pressures indicate that these compounds could evaporate from aquatic systems.

Before a full assessment of the hazard posed by these compounds could be undertaken, extensive data would need to be produced concerning their likely fate and distribution.

3.3 Summary

- The structures of nine flame retardants, formed from the dimerization of HCCPD are known and there is evidence of impurities in some of these compounds.
- Dechlorane Plus largely succeeded Dechlorane (mirex) as a flame retardant in polymer systems and was the major flame retardant of this class of compounds imported for use in Canada.
- A detailed survey is available on the quantities of the various Dechloranes that have been used in Canada. The survey shows that several companies have small quantities in inventory awaiting disposal.
- The Mirex Task Force report concluded that "very small amounts of both mirex and Dechlorane Plus are entering the Speed River at Cambridge. A low concentration of Dechlorane Plus was detected in the Credit River." No further data are available concerning the routes of entry or levels of Dechloranes in the Canadian environment.
- The Hooker Chemical Corporation tests show that the Dechloranes have low oral, dermal, inhalation and ocular toxicity. These compounds do not appear to have a degree of biological activity in any way comparable to the cyclodiene insecticides. For a full assessment of these compounds further toxicological data are needed.
- Only mirex and Dechlorane 602 were accumulated in fish from water. Dechlorane Plus, 603 and 604 were not appreciably accumulated from water. All the Dechloranes were accumulated by fish from food; Dechlorane Plus was least accumulated.
- Dechlorane Plus did not biodegrade in microbial test systems. Other Dechloranes have not been tested for biodegradability.
- Information is lacking by which to assess the likely fate and distribution of Dechloranes released into the environment.

4 INFORMATION GAPS - RECOMMENDATIONS

Recommendations that certain investigations should be undertaken with regard to HCCPD adducts, particularly Dechloranes other than mirex were reported in Appendix 3 (p. 149) of the "Task Force on Mirex" report.

The first recommendation concerned notification by those involved with Dechloranes. The second of the Task Force recommendations concerned the collection of detailed information on the quantities of material used or processed on a retrospective basis. These two recommendations were acted upon and provided the information presented in Section 2 of this report. The third recommendation stated:

"The published information concerning the organohalogen Dechloranes and their transformation products is not well developed. It is recommended that if their use continues, and adequate toxicological data cannot be obtained from existing sources, extensive toxicology testing be undertaken on the organohalogen Dechloranes and their transformation products to assess their long-term effects on human health and other organisms in the environment.

Part of the toxicological evaluation of substances is concerned with their physical-chemical properties and the prediction of their probable behaviour in the environment, to assess the likelihood and severity of exposure. It is recommended that appropriate studies be initiated to evaluate the probable behaviour of the organohalogen Dechloranes in the environment."

The toxicological aspects of this recommendation have not been implemented. There is still a need for detailed toxicological testing. It is recommended that a detailed protocol be formulated to describe the toxicological testing that should be undertaken if Dechloranes are to continue use in Canada.

Some aspects of the chemodynamics of Dechloranes have been investigated, notably the persistance in the aquatic environment and the pharmacokinetics in fish. Basic data, such as vapour pressure, solubility or photolytic properties, by which to assess the environmental significance of Dechloranes are not available. It is recommended that if Dechloranes are to continue in use in Canada, a testing protocol should include provision for chemodynamic information.

The available information indicates that Dechloranes are extremely insoluble and are unlikely to be accumulated by fish by direct uptake. One possible critical pathway might be through uptake of Dechloranes by benthic organisms after sedimentation of the material from the water. Secondary consumers might concentrate these compounds from benthic organisms resulting in possible human exposure. Any testing protocol developed for these compounds would need to address these concerns.

Most of the Dechloranes are incorporated within a plastic matrix and will eventually be discarded in landfill. The leaching of Dechloranes from plastics has not been studied. This route into the environment could permit the entry of this compound over a prolonged period of time. Very little research on this aspect of environmental contamination has been undertaken. If a protocol for testing Dechloranes is drawn up it should include a methodology for investigating leaching of these compounds from plastics.

The fourth and fifth recommendations of the Task Force on Mirex were concerned with further research and investigations that the government should undertake. They concerned monitoring Lake Ontario and the Niagara and St. Lawrence Rivers for the sources and extent of contamination with organohalogen alicyclic substances. The implications of this contamination for human health and organisms in the environment should be assessed. Specifically recommended were monitoring and surveillance of the amounts of Dechloranes discharged in effluents and emissions in the Lake Ontario ecosystem, investigations of industrial plants using Dechloranes, effects on wild fish populations and investigations of the methods for safe disposal.

Very little work has been undertaken on these recommendations because Dechloranes have not been found extensively in the environment and have only been found close to locations where they have been used. They have not been found in biota even close to industrial plants using them. Based on the existing evidence, there does not appear to be a requirement to implement these recommendations except for the investigation of industrial plants and methods for safe disposal.

The sixth recommendation of the Task Force on Mirex concerned human exposure research and epidemiology. It referred particularly to people who might have a high proportion of Lake Ontario fish in their diets or who might be occupationally exposed to Dechloranes. Dechloranes do not appear to be bioconcentrated to any large degree; therefore, the recommendation concerning epidemiology of consumers of Lake Ontario fish is not justified.

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APPENDIX

THE TOXICOLOGY OF DECHLORANE PLUS, 602, 603 AND 604

APPENDIX THE TOXICOLOGY OF DECHLORANE PLUS, 602, 603 AND 604

The toxicology of Dechlorane fire retardants has been summarized in trade memoranda by the Hooker Chemical Corporation and is pharaphrased or reprinted below.

Dechlorane Plus

Mammals

In acute oral toxicity studies on rats the LD_{50} was calculated to be greater than 25 g/kg. The acute dermal toxicity to albino rabbits was greater than 8 g/kg. In studies of the acute inhalation toxicity to rats the LC_{50} was greater than 2.25 mg/L of air.

In a subacute study, feeding Dechlorane Plus to rats for 90 days, no study-related mortalities were noted during the experiment. At the 100 000 ppm feeding level, liver to body weight ratios were significantly increased, but no changes were noted at 10 000 or 30 000 ppm. No treatment-related differences were noted for hematologic or urine analysis, for gross pathology or histopathologic examination.

In a 28-day study of dermal toxicity to albino rabbits no animals died, even at the 2 000 mg/kg dose level. Hematology and clinical blood chemistry were normal as were the gross and microscopic pathologic studies. In females, the gonad weight at the 500 mg/kg and 2 000 mg/kg level, and the liver weight at the 2 000 mg/kg level, were decreased. This was considered to be due to chance groupings in a small number of animals per treatment (5 males and 5 females per treatment).

A 28-day toxicity study of the effects of inhalation of Dechlorane Plus dust on rats showed no effect on body weight, hematologic parameters, clinical chemistry or urinalysis. Males and females in both test groups exhibited higher than normal absolute liver weights. Lung weights were also higher than normal for females in the test groups and males at the higher dose level. Organ to body weight was also significantly higher for males at the higher dose level. Gross pathologic examinations revealed no tissue alterations attributable to the test material. Lungs exhibited slightly increased numbers of macrophages in the alveoli of treated animals over the controls. Hepatocytomegaly of centrilobular hepatocytes were present in all male rats of the test group and two of the females of the high dose level. These alterations were associated with enlargement of hepatocytes with a "ground glass" appearance of the cytoplasm. These latter effects were considered to be effects of inhalation of Dechlorane Plus dust. No other histopathologic

alterations attributable to the test material were observed. It was concluded that the effects noted above in the lung and liver are to be considered as effects of the Dechlorane Plus when animals are exposed to extended periods of inhalation of the dust.

In an eye irritation study one mL portions of the test material were placed into the right eye of each of nine test rabbits. The test group was divided equally into three groups as described below:

Group A Right eye unwashed after application of test material.
Group B Right eye washed 4 seconds after application.
Group C Right eye washed 2 seconds after application.

The left eye of each animal served as the control. The test material did not produce corneal, iridial, or conjunctival effects in any of the animals. Dechlorane Plus, as tested, is not determined to be an ocular irritant.

In a skin sensitization test using guinea pigs, Dechlorane Plus was not found to cause irritation at the site of initial application, nor at a challenge site.

Fish

In a 96-hour toxicity study, four groups of 10 young bluegills were exposed to levels between 0.1 ppm and 100 ppm in static test chambers. No mortalities were observed among the treatments.

Dechlorane 602

Acute Oral Dose Range - Rats

The test material was administered by gastric intubation to groups of male albino rats of the Carworth (Sprague-Dawley derived) strain. The animals weighed, at initiation, from 170 to 250 g.

Following a two-hour fasting period, a single dose of test material was administered to six groups of two male rats each. Dosage levels were 31.6, 100, 316, 1 000, 3 160, and 10 000 mg/kg of body weight.

Postdose diet consisted of readily available Purina Laboratory Chow and water. The animals were observed daily for mortality and toxic effects for three days, after which they were sacrificed and discarded.

No deaths or toxic signs were noted at any of the dosage levels tested; therefore, the acute oral LC_{50} of Dechlorane 602 was assumed to be greater than

10 000 mg/kg of body weight. Dechlorane 602 could be classified as being practically nontoxic by the oral route.

Acute Dermal Application - Rabbits

The test animals were four groups of two adult albino rabbits of the New Zealand White variety. The animals weighed, at initiation, 1.9 to 3.2 kg.

A single application of the test material was made at dosage levels of 215, 464, 1 000, and 2 150 mg/kg of body weight. The test material was applied to the pre-moistened (tap water) and closely clipped intact (half the animals) or abraded (half the animals) abdominal skin of each rabbit beneath a binder of freezer paper. The trunk of each animal was then wrapped with gauze and adhesive tape, and a collar was placed around the neck of each animal to preclude ingestion of the material. After an exposure period of 24 hours, the binders were removed, and the abdominal skin was cleansed with tap water. Purina Rabbit Chow and water were readily available to the animals throughout the test period.

Mortality and toxic effect were recorded immediately following the application, at 24 hours, and once daily thereafter for a total of seven days. Dermal irritation was recorded at 24 hours for all dosage levels and once daily thereafter for a total of seven days. Additionally, the amount of compound residue present at 24 hours was estimated. Body weights, in all cases, were recorded both initially and terminally.

Following a seven-day observation period, all surviving animals were to be sacrificed via intravenous air embolism and necropsied. As well, necropsies were to be performed on any animals that succumbed during the course of the study.

No deaths occurred at any dosage level; therefore, the LD_{50} was assumed to be greater that 2 150 mg/kg of body weight. No toxic effects were noted.

A small amount of residue was present on the binders or abdomen following removal of the binders at 24 hours.

Slight signs of dermal irritation were noted; slight erythema was noted at 24 hours on the abrasions at abraded sites at the two lower levels and continued until day 3 (464 mg/kg level). Slight desquamation on abrasions was also observed on the abraded site at the 215 mg/kg level from day 3 through termination.

Major necropsy findings included white foci on the lobes of liver at sacrifice at the three higher levels. A slightly enlarged kidney was observed at the 464 mg/kg level.

The results of this test suggest that Dechlorane 602 could not be considered a primary irritant.

Acute Eye Irritation - Rabbits

The test animals were three adult rabbits of the New Zealand variety. At initiation, the animals weighed from 1.9 to 2.2 kg.

Prior to the test, the eyes of all subject animals were judged to be free of irritation and corneal damage as confirmed by sodium fluorescein examination. A single application of 100 mg of the test material was made into the left conjunctival sac of each of the three rabbits. Treated eyes were held closed for one second following application. Untreated eyes served as controls.

The animals were observed for gross signs of irritation and systematic toxicity at 1, 4, 24, 48, 72 and 96 hours following application. Eye irritation was graded and scored according to Draize, J.H. from the "Appraisal of the Safety of Chemicals in Foods, Drugs, and Cosmetics," Association of Food and Drug Officials of the U.S., Austin, Texas, (1959). Body weights were recorded initially and terminally.

A terminal fluorescein examination was performed on all three rabbits on day 4 (96 hours after initiation).

Slight conjunctival erythema was observed at 24 hours only. The compound was still in the eyes of two rabbits at 24 hours.

Acute Inhalation Toxicity - Rats

Four groups of animals, each consisting of three male and three female rats, were exposed for one hour to the aerosol of the test material. In addition, three male and three female rats were exposed under experimental conditions to filtered room air for one hour. They served as a control. The mean body weights of all animals were determined prior to exposure.

The exposures were conducted in a 100 L, stainless steel and plexiglass chamber under semi-closed conditions. The experimental atmosphere was generated by aerosolizing and metering the compound into the chamber by means of aerodynamic, DeVilbiss powder blowers. The chamber airflow was produced and maintained by a positive pressure rotary pump located on the exhaust side of the chamber and was monitored by a rotameter. In order to attain the maximum concentration, the total airflow was adjusted so as to equal the airflow introduced into the chamber by the

DeVilbiss blowers. The nominal concentration of test material in the experimental atmosphere was calculated from the ratio of the weight of the compound aerosolized to the total chamber airflow per unit time.

During exposure, the animals were housed individually in stainless steel cages centered in the chamber on a rack. They were observed at frequent intervals for death or signs of irritation.

After exposure, the animals were removed from the chamber and group housed by sex. They were observed daily for seven days for latent toxic effects. Terminal body weights of all survivors were determined. Gross necropsies were performed on all animals. All major organs were removed, examined for gross lesions, and preserved in 10% buffered formalin for possible future histological examination.

Control Exposure: No signs of irritation were seen in the animals either during exposure or during the seven-day observation period. The mean body weights of the rats (in grams) were as follows:

Sex	Number of Animals	Mean Body Weight (grams) Pre-exposure	Termination
Male	3	310	335
Female	3	238	246

Gross necropsy findings included red to brown areas of discolouration on the lungs.

Dechlorane 602 Exposure: A total of 55 g of Dechlorane 602 was aerosolized and introduced into the chamber during the one-hour exposure. Airflow through the chamber was maintained at 10 L/min. Thus, the nominal concentration of Dechlorane 602 in the experimental atmosphere was calculated to be 91 mg/L of air.

The animals remained inactive throughout the exposure. The eyes were partially or completely closed after 10 minutes of exposure. After 55 minutes of exposure, the respiration of the animals was slightly shallow. All rats appeared normal when returned to group housing and remained so throughout the seven-day observation period. The mean body weights of the rats were as follows:

Sex	Number of Animals	Mean Body Weight (grams) Pre-exposure	Termination
Male	3	257	305
Female	3	217	217

Gross necrospy findings include red to brown areas of discolouration on the lungs and dark purple to black renal medullae.

Dechlorane 602 was deemed to be relatively nontoxic under the test conditions described.

Dechlorane 603

Acute Oral Dose Range - Rats

The test material was administered by gastric intubation to groups of male albino rats of the Carworth (Sprague-Dawley derived) strain. The animals weighed, at initiation, from 170 to 250 g.

Following a two-hour fasting period, a single dose of test material was administered to six groups of two male rats each. Dosage levels were 31.6, 100, 316, 1 000, 3 160, and 10 000 mg/kg of body weight.

Postdose diet consisted of readily available Purina Laboratory Chow and water. The animals were observed daily for mortality and toxic effects for three days, after which they were sacrificed and discarded.

No deaths or toxic signs were noted at any of the dosage levels tested; therefore, the acute oral LD_{50} of Dechlorane 603 was assumed to be greater than 10 000 mg/kg of body weight. Dechlorane 603 could be classified as being practically nontoxic by the oral route.

Acute Dermal Application - Rabbits

The test animals were four groups of two adult albino rabbits of the New Zealand White variety. The animals weighed, at initiation, 1.9 to 3.2 kg.

A single application of the test material was made at dosage levels of 215, 464, 1 000, and 2 150 mg/kg of body weight. The test material was applied to pre-moistened (tap water) and closely clipped intact (half the animals) or abraded (half the animals) abdominal skin of each rabbit beneath a binder of freezer paper. The trunk of each animal was then wrapped with gauze and adhesive tape, and a collar was placed

around the neck of each animal to preclude ingestion of the material. After an exposure period of 24 hours, the binders were removed and the abdominal skin was cleansed with tap water. Purina Rabbit Chow and water were readily available to the animals throughout the test period.

Mortality and toxic effects were recorded immediately following the application, at 24 hours, and once daily thereafter for a total of seven days. Dermal irritation was recorded at 24 hours for all dosage levels and once daily thereafter for a total of seven days. Additionally, the amount of compound residue present at 24 hours was estimated. Body weights, in all cases, were recorded both initially and terminally.

Following a seven-day observation period, all surviving animals were to be sacrificed via intravenous air embolism and necropsied. Necropsies were to be performed on any animals that succumbed during the course of the study.

One death occurred at the 2 150 mg/kg level on day 2. Since no prior dermal effects were noted, the death was assumed to be due to incidental causes; therefore, the LD_{50} was estimated to be greater than 2 150 mg/kg of body weight. The only incidence of toxic effects observed was diarrhea occurring at 14 hours in one animal at the 2 150 mg/kg level prior to death on day 2.

Slight to moderate signs of dermal irritation were noted. Slight to moderate erythema on abrasions of abraded sites at the three higher levels was observed at 24 hours and generally subsided by day 4. Slight desquamation on abrasions of the abraded site was also observed at the 2 150 mg/kg level from day 3 through termination.

A small to moderate amount of residue was present on the binders or abdomen following removal of the binders at 24 hours.

Acute Eye Irritation - Rabbits

The test animals were three adult albino rabbits of the New Zealand variety. At initiation, the animals weighed from 1.9 to 2.2 kg.

Prior to the test, the eyes of all subject animals were judged to be free of irritation and corneal damage as confirmed by sodium fluorescein examination. A single application of 100 mg of the test material was made into the left conjunctival sac of each of the three rabbits. Treated eyes were held closed for one second following application. Untreated eyes served as controls.

The animals were observed for gross signs of irritation and systematic toxicity at 1, 4, 24, 48, 72 and 96 hours following application. Eye irritation was graded and

scored according to Draize, J.H., from the "Appraisal of the Safety of Chemicals in Foods, Drugs, and Cosmetics," Association of Food and Drug Officials of the U.S., Austin, Texas, (1959). Body weights were recorded initially and terminally.

A terminal fluorescein examination was performed on all three rabbits on day 4 (96 hours after initiation).

Slight conjunctival erythema was noted by 24 hours and through 72 hours in all animals. One eye showed slight chemosis at 48 and 72 hours. Some Dechlorane 603 remained in one eye at 24 hours. Sodium fluorescein staining was negative for all animals on day 4.

Major necropsy findings included white foci throughout the mesentery at sacrifice at the 464 mg/kg level. The animal that died at day 2 showed no observable gross pathology due to advanced autolysis.

The results indicate that Dechlorane 603 could not be considered a primary irritant.

Acute Inhalation Toxicity - Rats

Four groups of animals, each consisting of three male and three female rats, were exposed for one hour to the aerosol of the test material. In addition, three male and three female rats were exposed under experimental conditions to filtered room air for one hour. They served as a control. The mean body weights of all animals were determined prior to exposure.

The exposures were conducted in a 100 L, stainless steel and plexiglass chamber under semi-closed conditions. The experimental atmosphere was generated by aerosolizing and metering the compound into the chamber by means of aerodynamic, DeVilbiss powder blowers. The chamber airflow was produced and maintained by a positive pressure rotary pump located on the exhaust side of the chamber and was monitored by a rotameter. In order to attain the maximum concentration, the total airflow was adjusted so as to equal the airflow introduced into the chamber by the DeVilbiss blowers. The nominal concentration of test material in the experimental atmosphere was calculated from the ratio of the weight of the compound aerosolized to the total chamber airflow per unit time.

During exposure, the animals were housed individually in stainless steel cages centered in the chamber on a rack. They were observed at frequent intervals for death or signs of irritation.

After exposure, the animals were removed from the chamber and group housed by sex. They were observed daily for seven days for latent toxic effects. Terminal body weights of all survivors were determined. Gross necropsies were performed on all animals. All major organs were removed, examined for gross lesions, and preserved in 10% buffered formalin for possible future histological examination.

Control Exposure: No signs of irritation were seen in the animals, either during exposure or during the seven-day observation period. The mean body weights of the rats (in grams) were as follows:

Sex	Number of Animals	Mean Body Weight (grams) Pre-exposure	Termination
Male	3	310	335
Female	3	238	246

Gross necropsy findings included red to brown areas of discolouration on the lungs.

Dechlorane 603 Exposure: A total of 33.3 g of Dechlorane 603 was aerosolized and introduced into the chamber during the one-hour exposure. Airflow through the chamber was maintained at 10 L/min. Thus, the nominal concentration of Dechlorane 603 in the experimental atmosphere was calculated to be 56 mg/L of air.

The animals remained quiet but alert throughout the exposure. After 20 minutes of exposure, the respiratory patterns of the animals appeared deep and slightly uneven. By the termination of the exposure, open-mouthed gasping was noted in one animal. All animals appeared normal throughout the seven-day observation period. The mean body weights of the rats were as follows:

Sex	Number of Animals	Mean Body Weight (grams) Pre-exposure	Termination
Male	3	295	317
Female	3	227	231

scored according to Draize, J.H., ... Foods, Drugs, and Cosmetics ... Texas, (1959). Body w... They included red to brown ...ed in control animals and in the

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...our fasting period, a single dose of test material was administered ... of two male rats each. Dosage levels were 31.6, 100, 316, 1 000, 3 160 and ... ...g/kg of body weight.

Postdose ...iet consisted of readily available Purina Laboratory Chow and water. The animals were observed daily for mortality and toxic effects for three days, after which they were sacrificed and discarded.

No deaths or toxic signs were noted at any of the dosage levels tested; therefore, the acute oral LD_{50} of Dechlorane 604 was assumed to be greater than 10 000 mg/kg body weight. Dechlorane 604 could be classified as being practically nontoxic by the oral route.

Acute Dermal Application - Rabbits

The test animals were four groups of two adult albino rabbits of the New Zealand White variety. The animals weighed, at initiation, 1.9 to 3.2 kg.

A single application of the test material was made at dosage levels of 215, 464, 1 000, and 2 150 mg/kg of body weight. The test material was applied to pre-moistened (tap water) and closely clipped intact (half the animals) or abraded (half the animals) abdominal skin of each rabbit beneath a binder of freezer paper. The trunk of each animal was then wrapped with gauze and adhesive tape, and a collar was placed around the neck of each animal to preclude ingestion of the material. After an exposure period of 24 hours, the binders were removed, and the abdominal skin was cleansed with tap water. Purina Rabbit Chow and water were readily available to the animals throughout the test period.

Mortality and toxic effects were recorded immediately following the application, at 24 hours, and once daily thereafter for a total of seven days. Dermal irritation was recorded at 24 hours for all dosage levels and once daily thereafter for a total of seven days. Additionally, the amount of compound residue present at 24 hours was estimated. Body weights, in all cases, were recorded both initially and terminally.

Following a seven-day observation period, all surviving animals were to be sacrificed via intravenous air embolism and necropsied. Necropsies were to be performed on any animals that succumbed during the course of the study.

No deaths occurred at any dosage level; therefore, the LD_{50} was assumed to be greater than 2 150 mg/kg of body weight. Slight terminal body weight loss was noted at the three higher levels, and soft feces observed in one animal at the 1 000 mg/kg level on day 5 only.

A small to moderate amount of residue was present on the binders or abdomen following removal of the binders at 24 hours.

Slight signs of dermal irritation were noted at 24 hours. Slight erythema on abrasions of abraded sites at all levels persisted until day 3. Slight erythema was also noted on one intact site at the 215 mg/kg level at 24 hours only. Slight desquamation was observed on abrasions of one abraded site at the 2 150 mg/kg level on day 5 only.

Major necropsy showed white foci on lobes of the liver at sacrifice at the 1 000 mg/kg level.

Based on the findings of this experiment, Dechlorane 604 could not be considered a primary irritant.

Acute Eye Irritation - Rabbits

The test animals were three adult albino rabbits of the New Zealand variety. At initiation, the animals weighed from 1.9 to 2.2 kg.

Prior to the test, the eyes of all subject animals were judged to be free of irritation and corneal damage as confirmed by sodium fluorescein examination. A single application of 100 mg of the test material was made into the left conjunctival sac of each of the three rabbits. Treated eyes were held closed for one second following application. Untreated eyes served as controls.

The animals were observed for gross signs of irritation and systematic toxicity at 1, 4, 24, 48, 72 and 96 hours following application. Eye irritation was graded and scored according to Draize, J.H. from the "Appraisal of the Safety of Chemicals in Foods,

Gross necropsy findings were not meaningful. They included red to brown areas of discolouration on the lungs similar to those noted in control animals and in the other test groups.

Dechlorane 603 was deemed to be relatively nontoxic under the test conditions described.

Dechlorane 604

Acute Oral Dose Range - Rats

The test material was administered by gastric intubation to groups of male albino rats of the Carworth (Sprague Dawley derived) strain. The animals weighed, at initiation, from 170 to 250 g.

Following a two-hour fasting period, a single dose of test material was administered to six groups of two male rats each. Dosage levels were 31.6, 100, 316, 1 000, 3 160 and 10 000 mg/kg of body weight.

Postdose diet consisted of readily available Purina Laboratory Chow and water. The animals were observed daily for mortality and toxic effects for three days, after which they were sacrificed and discarded.

No deaths or toxic signs were noted at any of the dosage levels tested; therefore, the acute oral LD_{50} of Dechlorane 604 was assumed to be greater than 10 000 mg/kg body weight. Dechlorane 604 could be classified as being practically nontoxic by the oral route.

Acute Dermal Application - Rabbits

The test animals were four groups of two adult albino rabbits of the New Zealand White variety. The animals weighed, at initiation, 1.9 to 3.2 kg.

A single application of the test material was made at dosage levels of 215, 464, 1 000, and 2 150 mg/kg of body weight. The test material was applied to pre-moistened (tap water) and closely clipped intact (half the animals) or abraded (half the animals) abdominal skin of each rabbit beneath a binder of freezer paper. The trunk of each animal was then wrapped with gauze and adhesive tape, and a collar was placed around the neck of each animal to preclude ingestion of the material. After an exposure period of 24 hours, the binders were removed, and the abdominal skin was cleansed with tap water. Purina Rabbit Chow and water were readily available to the animals throughout the test period.

Mortality and toxic effects were recorded immediately following the application, at 24 hours, and once daily thereafter for a total of seven days. Dermal irritation was recorded at 24 hours for all dosage levels and once daily thereafter for a total of seven days. Additionally, the amount of compound residue present at 24 hours was estimated. Body weights, in all cases, were recorded both initially and terminally.

Following a seven-day observation period, all surviving animals were to be sacrificed via intravenous air embolism and necropsied. Necropsies were to be performed on any animals that succumbed during the course of the study.

No deaths occurred at any dosage level; therefore, the LD_{50} was assumed to be greater than 2 150 mg/kg of body weight. Slight terminal body weight loss was noted at the three higher levels, and soft feces observed in one animal at the 1 000 mg/kg level on day 5 only.

A small to moderate amount of residue was present on the binders or abdomen following removal of the binders at 24 hours.

Slight signs of dermal irritation were noted at 24 hours. Slight erythema on abrasions of abraded sites at all levels persisted until day 3. Slight erythema was also noted on one intact site at the 215 mg/kg level at 24 hours only. Slight desquamation was observed on abrasions of one abraded site at the 2 150 mg/kg level on day 5 only.

Major necropsy showed white foci on lobes of the liver at sacrifice at the 1 000 mg/kg level.

Based on the findings of this experiment, Dechlorane 604 could not be considered a primary irritant.

Acute Eye Irritation - Rabbits

The test animals were three adult albino rabbits of the New Zealand variety. At initiation, the animals weighed from 1.9 to 2.2 kg.

Prior to the test, the eyes of all subject animals were judged to be free of irritation and corneal damage as confirmed by sodium fluorescein examination. A single application of 100 mg of the test material was made into the left conjunctival sac of each of the three rabbits. Treated eyes were held closed for one second following application. Untreated eyes served as controls.

The animals were observed for gross signs of irritation and systematic toxicity at 1, 4, 24, 48, 72 and 96 hours following application. Eye irritation was graded and scored according to Draize, J.H. from the "Appraisal of the Safety of Chemicals in Foods,

Drugs, and Cosmetics," Association of Food and Drug Officials of the U.S., Austin, Texas (1959). Body weights were recorded initially and terminally.

A terminal fluorescein examination was performed on all three rabbits on day 4 (96 hours after initiation).

Two rabbits showed slight conjunctival erythema by 24 hours and through 72 hours. One eye had retained some Dechlorane 604 at 24 hours and had white exudate in the left corner at 72 hours.

Acute Inhalation Toxicity - Rats

Four groups of animals, each consisting of three male and three female rats, were exposed for one hour to the aerosol of the test material. In addition, three male and three female rats were exposed under experimental conditions to filtered room air for one hour. They served as a control. The mean body weights of all animals were determined prior to exposure.

The exposures were conducted in a 10 L, stainless steel and plexiglass chamber under semi-closed conditions. The experimental atmosphere was generated by aerosolizing and metering the compound into the chamber by means of aerodynamic, DeVilbiss powder blowers. The chamber airflow was produced and maintained by a positive pressure rotary pump located on the exhaust side of the chamber and was monitored by a rotameter. In order to attain the maximum concentration, the total airflow was adjusted so as to equal the airflow introduced into the chamber by the DeVilbiss blowers. The nominal concentration of test material in the experimental atmosphere was calculated from the ratio of the weight of the compound aerosolized, to the total chamber airflow per unit time.

During exposure, the animals were housed individually in stainless steel cages centered in the chamber on a rack. They were observed at frequent intervals for death or signs of irritation.

After exposure, the animals were removed from the chamber and group housed by sex. They were observed daily for seven days for latent toxic effects. Terminal body weights of all survivors were determined. Gross necropsies were performed on all animals. All major organs were removed, examined for gross lesions, and preserved in 10% buffered formalin for possible future histological examination.

Control Exposure: No signs of irritation were seen in the animals, either during exposure or during the seven-day observation period. The mean body weights of the rats (in grams) were as follows:

Sex	Number of Animals	Mean Body Weight (grams) Pre-exposure	Termination
Male	3	310	335
Female	3	238	246

Gross necropsy findings included red to brown areas of discolouration on the lungs.

Dechlorane 604 Exposure: A total of 69.0 g of Dechlorane 604 was aerosolized and introduced into the chamber during the one-hour exposure. Airflow through the chamber was maintained at 10 L/min. Thus, the nominal concentration of Dechlorane 604 in the experimental atmosphere was calculated to be 115 mg/L of air.

Preening and a mastication-like movement were observed in the animals after five minutes of exposure. This continued intermittently for the duration of the exposure. All animals' eyes were partially or completely closed after 25 minutes of exposure. All rats appeared normal when they were returned to group housing following exposure and remained so throughout the seven-day observation period. The mean body weights were as follows:

Sex	Number of Animals	Mean Body Weight (grams) Pre-exposure	Termination
Male	3	295	289
Female	3	233	232

Gross necropsy findings included red to brown areas of discolouration on the lungs.

Dechlorane 604 was deemed to be relatively nontoxic under the test conditions described.